Clinical and prognostic relationships of pulmonary artery to aorta diameter ratio in patients with heart failure. A cardiac magnetic resonance imaging study.

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Abstract

Background: The pulmonary artery (PA) distends as pressure increases. The ratio of PA to aortic (Ao) diameter may be an indicator of pulmonary hypertension and consequently carry prognostic information in patients with chronic heart failure (CHF).

Methods: Patients with CHF and control subjects undergoing cardiac magnetic resonance imaging (CMRI) were evaluated. The main PA diameter and the transverse axial Ao diameter at the level of bifurcation of the main pulmonary artery were measured. The maximum diameter of both vessels was measured throughout the cardiac cycle and the PA/Ao ratio was calculated.

Results: 384 patients (mean age 69 years, mean left ventricular ejection fraction 40%, median amino terminal pro-brain natriuretic peptide (NTproBNP) 1,010 (IQR: 448-2,262) ng/l) and 38 controls were included. Controls and patients with CHF had similar maximum Ao and PA diameters, and PA/Ao ratio.

During a median follow up of 1,759 days (998-2,269), 181 patients with HF were hospitalised for HF or died. Neither PA diameter nor PA/Ao ratio predicted outcome in univariable analysis. In a multivariable model, only age and NT-proBNP were independent predictors of adverse events.

Conclusions: the PA/Ao ratio is not a useful method to stratify prognosis in patients with heart failure.

Introduction

For patients with chronic heart failure (CHF), pulmonary hypertension (PHT), right ventricular (RV) dysfunction and increased venous pressure and congestion are associated with a poor prognosis whether or not left ventricular ejection fraction (LVEF) is reduced [1-8].

An enlarged main pulmonary artery (PA) and an increased pulmonary/aorta (PA/Ao) diameter ratio are indirect signs of pulmonary hypertension (PHT) [9-11]. Their clinical and predictive value has been mainly studied in patients with respiratory diseases, including chronic obstructive pulmonary disease (COPD) [12-14] and pulmonary arterial hypertension [11, 15]. Previous studies suggest that the PA/Ao ratio, as assessed on computed tomography (CT), may be a useful measure of pulmonary hypertension, especially in patients younger than 50 years [16]. A PA/Ao ratio >1 detected by CT is also a powerful predictor of severe COPD exacerbations [12]. However, the clinical and prognostic utility of this measure in patients with CHF is unknown.

We therefore studied the association between PA/Ao diameter ratio and both clinical characteristics and outcome in patients with HF using cardiac magnetic resonance imaging **(**CMRI).

Methods

Study population

This is a single-centre prospective observational study. Between June 2005 and November 2011, ambulatory patients referred with suspected HF to a community HF clinic who had undergone CMRI as part of their investigation were enrolled. The analysis plan was designed post-hoc: the scans were not performed specifically to determine PA/Ao diameter ratio. Patients were followed up until 1st June 2015. Physical examination, routine laboratory tests (including NTproBNP), and electrocardiogram (ECG) were performed on the same day. Heart failure was defined as LVEF <50% on CMRI or plasma concentration of amino-terminal pro-B-type natriuretic peptide (NTproBNP) >220 pg/ml, consistent with the 2007 ESC consensus statement for diagnosis of heart failure with preserved ejection fraction [17].

A congestion score based on lung auscultation (normal, basal, mid zone, or diffuse crepitations), jugular venous pressure (not raised, raised 1-4 cm, up to the earlobe), peripheral oedema (none, ankles, below or above knees), and liver (not palpable, palpable) with one point attributed for each degree of severity was used. Patients with a score ≥3 were defined as being congested [18].

Data regarding deaths and hospitalisations were collected from the hospital's electronic systems, supplemented by information from patients, discharge letters, and their family doctors. Our hospital is the only one in the region offering acute medical services. We have access to both primary and secondary care records. Outcome was censored at the point of last medical contact in primary or secondary care. The vital status of all patients who had no local medical contact in the previous 6 months was ascertained from national records. The primary outcome was a composite of hospitalization for HF and all-cause mortality. Hospitalisations were considered to be HF related if the diagnosis was included in the death or discharge documentation, and if the discharge letter supported HF as a key reason for admission.

The study conformed to the principles outlined in the Declaration of Helsinki and was approved by relevant ethical bodies. Written informed consent was obtained from each patient.

Cardiac magnetic resonance imaging measurements

Cardiac magnetic resonance images were acquired using a 1.5 T scanner (either Sigma CV/I, GE Medical Systems or Achieva, Philips Medical Systems) equipped with a phased-array coil placed over the praecordium. ECG-gated cine acquisitions were performed during breath-hold (in expiration), using a steady state free precession pulse sequences in two standard long axes and multiple short-axis slices, with slice thickness of 8 mm and inter-slice distance of 2 mm from the base to the apex of the heart.

Images were analysed offline using QMass MR software (MEDIS, Leiden, The Netherlands). The multi-slice, short-axis cine data-sets were analysed to calculate left ventricular (LV) and right ventricular (RV) volumes and masses. Endocardial and epicardial borders were traced manually by an experienced observer using end-diastolic and end-systolic frames in contiguous short-axis slices. LV end-diastolic (EDV) and end-systolic (ESV) volumes were calculated using summation of area × [slice thickness + interslice gap] for each slice (Simpson's method), which were then used to calculate LVEF and LV mass. Papillary muscles were excluded from LV volume measurements and included in mass calculations. The interventricular septum was considered to be part of the LV. RV volumes, mass and EF were calculated in a similar fashion. Left atrium (LA) maximum volume was measured at the frame just before mitral valve opening in the 4 chamber long axis view. Mitral and tricuspid regurgitation volume was visually graded as none or trivial (0), mild (1) or moderate or worse (2). Intra and inter-variability data for CMRI measurements in our department have been reported [19].

The transverse axial diameter of the main pulmonary artery and the ascending aorta at the level of the bifurcation of the main pulmonary artery were measured by a single research fellow specializing in cardiovascular imaging (AU). The PA/Ao ratio was calculated as the ratio of their maximum diameters during the cardiac cycle (figure 1).

Statistical analysis

Categorical data are presented as number and percentages; normally distributed continuous data as mean ±SD; non-normally distributed variables as median and interquartile range (IQR). Independent samples t-tests, one-way ANOVA and Kruskal-Wallis tests were used to compare continuous variables between groups, and chi-squared tests were used for categorical variables.

Simple and multiple linear regression models were used to identify variables associated with PA/Ao ratio. Only the variables associated with PA/Ao in univariable analysis were entered into the multivariable analysis. Log transformation of NTproBNP and urea were used to satisfy the model assumptions. Associations between variables and prognosis were assessed using Cox proportional hazards models. Only variables associated with outcome ($p<0.1$) in univariable analysis were entered into multivariable models. Treatment variables were not included in the model as these are confounded by indication (patients who are sicker may be more likely to receive some treatments and less likely to tolerate others) and vary over time. Kaplan–Meier curves with the log-rank statistic were used to illustrate outcome. Analyses were performed using SPSS (v22) and Stata software, a two-sided P-value of 0.05 was considered statistically significant.

Results

Patient characteristics

Of 422 patients enrolled, 384 met the criteria for heart failure. The other 38 subjects were taken to be controls. Compared to controls, patients with HF were older, and were more likely to have ischaemic heart disease (IHD) and atrial fibrillation (AF). Their demographic and clinical characteristics are shown in Table 1.

PA and Ao diameters, and their ratio, were similar in patients with HF and controls. Amongst patients with HF, those in the highest tercile of PA/Ao ratio (greater PA/Ao ratio) were younger, had more severe symptoms and overall more congestion than the other two terciles.

Those in the highest PA/Ao tercile had both larger PA diameter and smaller Ao diameters on average. They also had larger LA and RV end diastolic volumes (Table 1).

Of the MRI variables, increasing RVEDV was most strongly associated with increasing PA/Ao ratio. Only decreasing age, and increasing LA and RV volumes were independently associated with increasing PA/Ao ratio (table 2). In patients with LVEF ≤ 40%, only decreasing age independently predicted a greater PA/Ao ratio, whilst in patients with LVEF > 40%, decreasing age and creatinine levels were associated with increasing PA/Ao ratio.

PA/Ao ratio was similar in men and women and in patients with or without COPD. Patients with more severe symptoms and congestion, and those with a clinically higher JVP had a greater PA/Ao ratio (Supplementary Table 1).

PA/Ao ratio and outcome

During a median follow-up of 1,759 days (IQR: 998-2,269) days (censored at time of first event) the primary outcome (hospitalization for HF and all-cause mortality) was reached by 47% (n=181) of patients with CHF and 29% (n=11) of controls. Neither minimum nor maximum PA and Ao diameter, nor their ratio, were associated with adverse outcomes in univariable analysis, even when PA diameter was indexed for body surface area (BSA; BSA is closely related to an adverse outcome in this, and in a larger dataset [20]). The only CMRI predictors of adverse events were greater LA volume, and lower LA and RV ejection fractions. In a multivariable model, including CMRI variables, only increasing age and NT-pro BNP were independent predictors of an adverse outcome (table 3).

There was no difference in outcome between patients who had PA/Ao >1 compared to ≤1 (HR: 1.07, 95% CI: 0.74-1.60, p=0.67) or between patients who had PA/Ao ≥0.9 versus <0.9 ((HR: 1.02, 95% CI: 0.76-1.37, p=0.90). Even when patients with a dilated ascending Ao (>4 cm) were excluded (n=25), results did not change substantially (PA/Ao >1versus ≤1 (HR: 1.05, 95% CI: 0.71-1.56, p=0.80); PA/Ao ≥0.9 versus <0.9 (HR: 0.97, 95% CI: 0.71-1.30, p=0.82). There was no difference in the primary outcome amongst the three PA/Ao terciles (figure 2).

During the study 147 patients died; neither minimum nor maximum PA (HR: 0.99, 95% CI: 0.95-1.03, p=0.55), maximum Ao diameter (HR: 0.99, 95% CI: 0.96-1.03, p=0.75), nor their ratio (HR: 0.82, 95% CI: 0.24-2.78, p=0.75), were associated with all-cause mortality.

Discussion

Measurement of the PA/Ao ratio may be of prognostic value in patients with respiratory disease [12, 21]. However, although we found that for patients with HF, a higher PA/Ao ratio measured by CMRI was associated with more clinical evidence of congestion, and larger left atrial and right ventricular volumes, it was not an important predictor of an adverse outcome.

Nakanishi and colleagues studied 1,326 patients undergoing coronary CT angiography for suspected coronary artery disease [22]. Consistent with our results, those with larger PA/Ao ratio were younger, and had a smaller aorta, but Nakanishi found that an elevated PA/Ao ratio (≥ 0.9) was an independent predictor of mortality. However, there were few death (58 compared to 147 in our study) with only 15 deaths in patients with a PA/Ao $\geq$0.9. They excluded patients with a dilated aorta (>4 cm) but excluding such patients did not improve prediction in our analysis.

There is a linear association between aortic size and increasing age [23], and increasing aortic size is associated with decreased distensibility [24]. Our finding of an inverse correlation between PA/Ao ratio and age is consistent with a previous study of 3,176 patients from the Framingham Heart Study which showed that the PA/Ao was lower in older participants [25].

Limitations

This was a single centre study and a retrospective analysis of data collected primarily for other purposes. Our findings should be prospectively tested before being considered definitive. The population enrolled in our study is not entirely representative of the heart failure population. Older patients with many co-morbidities and more advanced heart failure who might have a more dilated pulmonary artery are less likely to be referred for a CMRI, due to frailty, or contra-indications to a CMRI, such as an implanted pacemaker. Some authors might not accept an NTproBNP >220 pg/ml as diagnostic for heart failure with preserved ejection fraction, although it is consistent with ESC consensus statement available when the study was conceived [17].

Some might also argue that a control group consisting of symptomatic individuals with comorbidities which might cause heart failure is not appropriate for the initial evaluation of a method to stratify prognosis. Others will argue that a control population comprising conditions closely associated with heart failure, such as ours, is more relevant. The reader should decide. A control group of perfectly healthy older people would certainly be of interest, but unfortunately it was not locally available.

PA and Ao diameters were measured from axial images which in some cases were not planned exactly in line with the vessel orientation. This could have led to occasional under- or overestimations of the main artery diameters.

Invasive or non-invasive echocardiographic evaluation of PA pressure was not done at the time of the CMRI, so we do not know how many patients had PHT in this study.

Conclusions

Our findings suggest that a higher PA/Ao ratio is not a useful indicator of a poorer prognosis in patients with CHF. Publication of results from other centres would be of interest to confirm or refute our findings.

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Legend to figures.

Figure 1: An axial cardiac magnetic resonance imaging (cMRI) image at the level of pulmonary artery (PA) bifurcation, where measurements of the diameter of the main PA (in blue) and the diameter of the aorta (Ao, in red) were obtained to calculate PA/Ao ratio.

Figure 2: Kaplan Meier curve for the primary outcome of death from all causes and heart failure hospitalizations. There was no difference in the primary outcome for patients among the three PA/Ao terciles.

	No definite evidence of Heart Failure (38)	Evidence of Heart failure (384)	P-value	PA/Ao Tercile 1 (128)	PA/Ao Tercile 2 (128)	PA/Ao Tercile 3 (128)	P-value
Max Ao- mm	34.3 (31.4 - 36.9)	33.5 (30.8-36.3)	0.998	35.4 (33.1-38.4)	33.6 (31.2-35.7)	31.7 (28.9-34.0)	<0.001
Min Ao- mm	33.9 (30.4-36.4)	32.5 (29.5-35.1)	0.891	34.5 (31.9-37.1)	32.7 (30.19-34.7)	30.0 (28.2-33.1)	<0.001
Max PA- mm	28.8 (26.2-33.8)	29.4 (26.7-32.4)	0.934	26.3 (24.3- 28.8)	29.5 (27.3 32.1)	32.5 (29.7-35.7)	<0.001
Min PA- mm	25.1 (22.5-28.8)	25.9 (23.5-28.7)	0.585	23.8 (21.7-26.0)	25.9 (23.7- 28.0)	28.8 (26.1-31.5)	0.024
PA/Ao ratio	0.90 (0.77-0.99)	0.87 (0.79-0.97)	0.975	0.76 (0.71-0.79)	0.88 (0.85-0.92)	1.00 (0.97-1.07)	NA
Max PA/BSA	14.5 (13.1-15.8)	15.3 (13.9-16.7)	0.090	14.1 (12.6-15.2)	15.3 (14.0-16.4)	16.6 (15.4-18.3)	<0.001
Demographics							
Age – years	62 (11)	69 (11)	0.009	71 (9)	68 (11)	63 (12)	<0.001
Sex – male (%)	27 (71)	312 (81)	0.131	109 (85)	101 (79)	102 (80)	0.377
IHD – no. (%)	17 (44)	252 (65)	0.011	88 (69)	86 (67)	78 (61)	0.379
DM - no. (%)	9 (24)	104 (27)	0.652	26 (20)	38 (30)	40 (31)	0.104
Hypertension - no. (%)	23 (61)	196 (51)	0.264	70 (55)	68 (53)	58 (45)	0.275
COPD - no. (%)	4 (11)	27 (7)	0.431	11 (9)	8 (6)	8 (6)	0.699
NYHA class - no. (%)							
I	13(34)	77 (20)		28 (22)	27 (21)	22 (17)	
II	12(32)	180 (47)	0.080	72 (56)	53 (41)	55 (43)	0.019
III	13 (34)	140 (33)		28 (22)	48 (38)	51 (40)	
SBP – mmHg	135 (22)	133(25)	0.557	136(25)	133(24)	129(26)	0.083
Heart rate – bpm	70 (14)	67 (14)	0.172	67(12)	66 (15)	68 (16)	0.588
Atrial Fibrillation (%)	1 (3)	86 (22)	0.004	28 (22)	33 (26)	25 (29)	0.480
Congestion $\geq$ 3 – no.(%)	3 (8)	46 (12)	0.477	6 (5)	19 (15)	21 (16)	0.008
JVP – no. (%)							
raised 1-4 cm	0 (0)	29 (7)	0.167	4 (3)	9 (7)	16 (13)	0.026
up to the earlobe	0 (0)	5 (1)		0 (0)	3 (2)	2 (2)	
BMI - kg/m^2	32 (6)	28 (5)	0.002	28 (5)	29(5)	29 (6)	0.142
BSA – m^2	2.0 (0.2)	1.9 (0.2)	0.086	1.9 (0.2)	2.0 (0.2)	2.0 (0.2)	0.313
Blood test							
Haemoglobin – g/dl	14.1 (1.6)	13.5 (1.7)	0.032	13.7 (1.7)	13.3 (1.8)	13.6 (1.8)	0.221
Creatinine –µmol/l	94 (82-103)	99 (82-122)	0.012	102 (88-124)	105 (78-111)	92 (78-111)	0.036
Urea – mmol/l	5.6 (4.5-6.8)	6.5 (5.1-8.6)	0.023	7.0 (5.0-8.9)	6.5 (5.2-8.2)	6.2 (4.8-8.5)	0.387
Albumin - g/l	39 (3)	38 (3)	0.067	38 (3)	38 (3)	38 (4)	0.355
Bilirubin - µmol/l	14 (7)	16 (6)	0.315	16 (7)	15 (7)	16 (6)	0.371
NT-proBNP – ng/l	97 (49-154)	1010 (448-2262)	<0.001	875 (411-2326)	942 (449-2079)	1137 (463-2262)	0.959
Drugs							
Beta-blockers - no. (%)	19 (50)	306 (80)	<0.001	100 (78)	104 (81)	102 (80)	0.824

Ace-Inhibitors or ARB - no. (%)	28 (74)	336 (88)	0.018	113 (88)	110 (86)	113 (88)	0.807
Aldosterone Antagonist -no. (%)	10 (26)	139 (36)	0.224	45 (35)	48 (38)	46 (36)	0.924
Loop diuretics - no. (%)	16 (42)	263 (69)	0.001	81 (63)	90 (70)	92 (72)	0.289
MRI measurements							
LVEDV – ml	135 (113-156)	207 (163-254)	<0.001	200 (158- 242)	210 (162-265)	211 (172-257)	0.111
LVEF - %	60 (7)	40 (13)	<0.001	39 (31-48)	40 (31-46)	37 (29-48)	0.451
LV mass - g	115 (97-139)	145 (122-177)	<0.001	148 (124-181)	145 (123-179)	145 (120-174)	0.731
MAX LA volume – 4c - ml	69 (53-90)	106 (77-138)	<0.001	96 (67-127)	107 (79-140)	114 (79-148)	0.036
LAEF – 4ch - %	54 (48- 58)	40 (24-52)	<0.001	42 (27-53)	41 (27-52)	37 (20-52)	0.371
RVEDV – ml	154 (122-170)	146 (119-176)	0.518	135 (111-161)	147 (116-178)	156 (126-111)	0.005
RVEF - %	56 (49-58)	52 (44-60)	0.495	54 (45-60)	54 (47-60)	51 (40-60)	0.084
RV mass - g	46 (40-57)	51 (42-63)	0.341	49 (40-59)	51 (43-64)	54 (45-69)	0.017
Mitral regurgitation (%)							
Mild	8 (21)	149 (39)		48 (38)	46 (36)	55 (43)	0.769
Moderate/Severe	0 (0)	13 (3)	0.030	4 (3)	4 (3)	5 (4)	
Tricuspid regurgitation (%)							
Mild	8 (21)	100 (26)		28 (22)	32 (25)	40 (32)	0.384
Moderate/Severe	0 (0)	2 (1)	0.700	0 (0)	1 (1)	1 (1)	

Table 1: Characteristics of patients by diagnosis and, for patients with heart failure by terciles of pulmonary/aorta ratio. Data are mean and standard deviation if the variable is normally distributed and median and inter-tercile range if not. The statistical difference between variables is given for the comparison between patients with and without heart failure, and between terciles of PA/Ao only in patients with heart failure. List of abbreviation used: PA – Pulmonary Artery; Ao – Aorta; PA/Ao – Pulmonary/Aorta ratio; BSA: Body Surface Area; IHD - Ischemic Heart Disease; DM – Diabetes Mellitus; COPD - Chronic Obstructive Pulmonary Disease; NYHA – New York Heart Association; SBP - Systolic Blood Pressure; JVP - Jugular Vein Pressure; BMI - Body Mass Index; NT-proBNP - N-terminal B-type natriuretic peptide; ARB - Angiotensin receptor blocker; MRI- Magnetic Resonance Imaging; LVEDV - Left Ventricle End Diastolic Volume; LVEF – Left Ventricular Ejection Fraction; LV: Left Ventricle; LA – Left Atrium; LAEF - Left Atrial Ejection Fraction; RVEDV - Right Ventricle End Diastolic Volume; RVEF – Right Ventricular Ejection Fraction; RV - Right Ventricle. For right ventricular size and function, only 11 measurements were available for patients considered not to have heart failure and 313 for those considered to have heart failure.

PA/AO Ratio

Variables	Univariable analysis		Multivariable analysis Overall		Multivariable analysis LVEF ≤40%		Multivariable analysis LVEF >40%	
	Correlation coefficient	**p-value**	**Unstandardized Coefficients (95% CI)**	**T stat p-value**	**Unstandardized Coefficients with 95% CI**	**T stat p-value**	**Unstandardized Coefficients with 95% CI**	**T stat p-value**
Age - year	-0.311	<0.001	-0.004 (-0.005,-0.003) -0.005 (-0.006,-0.003)	-5.855; <0.001 -5.994; <0.001	-0.005 (-0.007,-0.003) -0.005 (-0.007,-0.003)	-4.776; <0.001 -4.615; <0.001	-0.003 (-0.005,-0.002) -0.004 (-0.006,-0.001)	-3.723; <0.001 -3.165; 0.002
SBP – mmHg	-0.108	0.035						
Heart rate - bpm	0.046	0.37						
BMI - kg/m^2	0.042	0.41						
BSA - m^2	0.032	0.53						
Creatinine –µmol/L	-0.095	0.06					0.000 (-0.001,0.000) -	-1.976; 0.05 -
Urea – mmol/l	-0.012	0.81						
Haemoglobin - g/dl	-0.034	0.50						
Albumin – g/l	-0.019	0.71						
Bilirubin – µmol/l	0.008	0.87						
Log(NT-proBNP)	0.028	0.058						
LVEDV – ml	0.108	0.034					- -0.001 (-0.001,0.000)	- -2.467; 0.015
LVEF - %	-0.047	0.36						
LV mass -g	-0.046	0.37						
LA Max – 4ch – ml	0.124	0.016	0.000 (0.000-0.001) -	2.623; 0.009 -				
LAEF – 4ch – %	-0.097	0.060						
RVEDV - ml	0.244	<0.001	- 0.001 (0.000-0.001)	- 2.484; 0.014			- 0.001 (0.000,0.002)	- 3.216; 0.002
RVEF - %	-0.148	0.009						
RV mass - g	0.133	0.019						

Table 2: Variables associated with PA/Ao ratio in patients with heart failure (n=384). Results were obtained from univariable and multivariable linear regression models. The first column on the left (Univariable analysis) represents the correlation between PA/Ao ratio and the variables studied. The column for the multivariable analysis (centre) shows the coefficients for slope of the linear relation between all the variables independently associated with PA/Ao for the overall population of patients with heart failure excluding (top; R^2=0.13, Adjusted R^2=0.11) or including (bottom; R^2=0.18, Adjusted R^2=0.15) measures of RV function (available for 313 patients only). On the right, the two different models were repeated for patients with LVEF $\leq$ 40% (RV excluded, R^2=0.16, Adjusted R^2 =0.13; RV included, R^2=0.17, Adjusted R^2 =0.13) and with LVEF> 40% (RV excluded, R^2=0.13, Adjusted R^2 =0.10; RV included, R^2=0.25, Adjusted R^2 =0.19). Variables included in multivariable models: age, LVEDV, LA max 4ch, SBP, Creatinine, Log NTproBNP (+ RVEDV, RVEDM, RVEF).

List of abbreviations used: LVEF – Left Ventricular Ejection Fraction; SBP - Systolic Blood Pressure; BMI - Body Mass Index; BSA – Body Surface Area; NTproBNP - N-terminal B-type natriuretic peptide; LVEDV - Left Ventricle End Diastolic Volume; LV- Left Ventricle; LA- Left Atrium; LAEF- Left Atrial Ejection Fraction; RVEDV- Right Ventricular End Diastolic Volume; RVEF- Right Ventricular Ejection Fraction; RV Right Ventricle.

Variables	Univariable analysis			Multivariable analysis		
	HR (95% CI)	χ^2	p-value	HR (95% CI)	χ^2	p-value
Clinical data						
Age - year	1.04 (1.03-1.06)	26.99	<0.001	1.02 (1.00-1.04)	5.89	0.015
Sex (Men)	1.07 (0.89-1.29)	0.49	0.48			
NYHA class (III vs. I/II)	1.58 (1.17-2.14)	9.04	0.003			
IHD (yes vs no)	1.28 (0.93-1.77)	2.28	0.13			
DM (yes vs no)	1.14 (0.82-1.58)	0.61	0.44			
COPD (yes vs no)	1.56 (0.95-2.58)	3.10	0.078			
AF (yes vs no)	1.06 (0.75-1.51)	0.11	0.74			
SBP – mmHg	0.99 (0.99-1.00)	0.16	0.69			
Heart rate - bpm	1.00 (1.00-1.01)	0.63	0.43			
BMI - kg/m^2	0.99 (0.96-1.02)	0.29	0.59			
BSA - m^2	0.41 (0.22-0.77)	7.74	0.005			
Congestion (≥3 vs <3)	1.55 (1.01-2.37)	4.05	0.044			
JVP (≥1 vs 0)	1.09 (0.65-1.83)	0.11	0.74			
Blood Test						
Creatinine –μmol/L	1.01 (1.00-1.01)	21.50	<0.001			
Urea – mmol/l	1.09 (1.05-1.12)	24.94	<0.001			
Haemoglobin - g/dl	0.82 (0.76-0.90)	19.91	<0.001			
Albumin – g/l	0.92 (0.89-0.95)	19.54	<0.001			
Bilirubin – μmol/l	1.00 (0.98-1.01)	0.27	0.60			
Log(NT-proBNP)	2.44 (1.79-3.32)	32.24	<0.001	1.66 (1.50-2.41)	7.18	0.007
MRI data						
LVEDV – ml	1.00 (0.99-1.01)	1.19	0.28			

LVEF - %	0.99 (0.98-1.00)	2.47	0.12
LV mass -g	1.00 (0.99-1.01)	0.97	0.32
LA Max – 4ch – ml	1.01 (1.00-1.01)	4.44	0.035
LAEF – 4ch – %	0.98 (0.97-0.99)	19.39	<0.001
RVEDV - ml	0.99 (0.99-1.00)	1.32	0.25
RVEF - %	0.99 (0.97-1.00)	3.96	0.047
RV mass - g	1.00 (1.00-1.01)	0.65	0.42
Min aorta- mm	0.99 (0.97-1.03)	0.11	0.75
Max aorta- mm	0.99 (0.95-1.02)	0.75	0.39
Max Pulmonary- mm	0.99 (0.96-1.03)	0.12	0.73
Min Pulmonary- mm	0.99 (0.98-1.01)	0.47	0.49
Pulmonary/Ao ratio	1.20 (0.41-3.49)	0.12	0.73
Max PA/BSA	1.05 (0.99-1.11)	2.32	0.13

Table 3: Univariable and multivariable Cox regression models for a combined endpoint of all-cause mortality and admissions for heart failure in patients with HF (n = 384 patients with heart failure who had 181 events during a median FU of 1759 (IQ 998-2269) days). Measurements of right ventricular size and function were not included in the multivariable analysis because these were available for only 313 patients (82%) with HF. LAEF only for patients in sinus rhythm with available data (n=298). Variables entered in multivariable models: Age, NYHA III vs I/II, COPD, BSA, Congestion, creatinine, Haemoglobin, Albumin, Log (NT-proBNP), LA max. List of abbreviation used: NYHA – New York Heart Association; IHD - Ischemic Heart Disease; DM – Diabetes Mellitus; COPD - Chronic Obstructive Pulmonary Disease; AF – Atrial Fibrillation; SBP - Systolic Blood Pressure; BMI - Body Mass Index; BSA: Body Surface Area; JVP – Jugular Vein Pressure; NT-proBNP - N-terminal B-type natriuretic peptide; LVEDV - Left Ventricle End Diastolic Volume; LVEF – Left Ventricular Ejection Fraction; LV - Left Ventricle; LA – Left Atrium; LAEF – Left Atrial Ejection Fraction; RV – Right Ventricle; PA – Pulmonary Artery.

Group	PA/Ao ratio		
	Characteristic Absent	Characteristic Present	**P value**
Male Sex	0.90 (0.12)	0.88 (0.14)	0.27
Diabetes Mellitus	0.88 (0.14)	0.90 (0.11)	0.36
COPD	0.89 (0.13)	0.87 (0.14)	0.44
IHD	0.91 (0.12)	0.88 (0.14)	0.06
NYHA III/IV	0.88 (0.14)	0.91 (0.12)	0.03
Congestion ≥3	0.88 (0.14)	0.93 (0.11)	0.006
JVP ≥1	0.88 (0.13)	0.94 (0.11)	0.004
Atrial fibrillation	0.89 (0.14)	0.88 (0.12)	0.68
Loop Diuretics	0.88 (0.14)	0.89 (0.13)	0.23
Mitral Regurgitation	0.88 (0.14)	0.89 (0.13)	0.50
Tricuspid Regurgitation	0.88 (0.14)	0.90 (0.12)	0.23

Table 1 Supplementary: Pulmonary/Aorta Ratio in patients with heart failure according to absence or presence of various patient and MRI characteristics. List of abbreviation used: PA/Ao- Pulmonary/Aorta; COPD - Chronic Obstructive Pulmonary Disease; IHD - Ischaemic Heart Disease; NYHA – New York Heart Association; JVP- Jugular Vein Pressure.